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cont.  
SUB H1)

87. The granule of claim 83, wherein the enzyme is a protease.

88. The granule of claim 83, wherein the enzyme is a cellulase.

ADD E57

#### REMARKS

In response to the office action dated July 25, 2000 finally rejecting all claims, Applicants are refiling the above-referenced application and submitting the instant preliminary amendment. Prior to this amendment claims 1 – 65 were pending in the application. Applicants have now cancelled claims 1 – 65 without prejudice, and are submitting new claims 66 – 88. The new claims are directed to granules comprising a matrix drawn to a combination of a protein (enzyme); a sugar or sugar alcohol; and a polysaccharide structuring agent. Original claims directed to a method of producing the granules, which were restricted by the Examiner in paper number 6, are being submitted in a further continuation application. Additionally, composition claims reciting a granule comprising a matrix drawn to a combination of a protein (enzyme); a sugar or sugar alcohol; and a polypeptide structuring agent, which were also restricted by the Examiner in paper number 6, have been canceled. Applicants submit new matter has not been introduced by the instant amendment.

New claims 66 and 83 are independent claims directed to a protein or enzyme granule wherein the granule comprises a seed particle and a matrix surrounding the seed particle. The matrix includes a combination of one or more proteins or enzymes, a sugar or sugar alcohol and a polysaccharide structuring agent. Support for claims 66 and 83 can be found in the original claims, specifically claims 1, 2, 7, 12, 18, 23, 24 and 29. Further support is found at pages 6 and 7 of the specification and in example 2. More specifically, the term "seed particle" is referred to at page 6 of the specification where it is disclosed that the matrix can be layered over a seed particle. The term seed particle is defined at page 6, lines 19 – 26. The preferred enzymes are disclosed at pages 8, lines 29 – 32 and 9, lines 1 – 8 of the specification. Claims 67 – 82 reciting a protein granule are dependent on claim 66, and claims 84 – 88 reciting an enzyme granule are dependent on claim 83.

In the final office action, the Examiner rejected Applicants' claims under 35 U.S.C. §102(b) as anticipated by Kiesser et al. (US Patent 5,739,091) and under 35 U.S.C. §102(b) as anticipated by Scott (EP 272 923). Claims 1, 7 – 11, 23, 29 – 33 were also rejected under 35 U.S.C. §103 as being unpatentable over Scott, and claims 1 – 3, 5, 6- 11, 23 – 25, 27 – 33 and 57 – 65 were rejected under 35 U.S.C. §103(a) as unpatentable over Markussen (EP 304 332).

Applicants' claimed granule comprises a seed particle and a matrix surrounding the seed particle. The matrix includes a protein (or enzyme) in combination with a sugar or sugar alcohol, and a polysaccharide structuring agent. For example, in one preferred embodiment as exemplified in example 2, the seed particle is composed of sodium sulfate crystals which are coated with a combination including an enzyme solution (protease), sucrose, and starch. The granule is further coated with one or more layers including methylcellulose, titanium dioxide, Neodol and PEG.

While the Kiesser et al. reference is directed to enzyme granules, Applicants contend the presently claimed invention is not anticipated by Kiesser et al. The Examiner states the Kiesser et al. granules,

".... comprise an enzyme or enzyme mixture, sugar, such as glucose, and a filler, such as cellulose. See column 1, lines 31 – 39, 60 – 67, column 2, line 66 to col.3, line 4. the granules may further comprise binders, such as polyethyleneglycol. See col. 2, lines 16 – 24. The granules may be covered with a protective coating (col. 4, lines 5 – 11). The coating can contain sugars (col. 4, lines 8 – 10) or polyethyleneglycol (col. 4, line 46). The granules may be prepared by layering the enzyme around dry-pre-mix. See col. 4, lines 21 – 24)."

As taught by the reference at column 1, lines 34 – 38, the enzyme granules comprise an enzyme or enzyme mixture, a water-insoluble filler mixture, water-soluble filler mixtures, binders, and if appropriate, other granulating auxiliaries, a formate of an alkali metal or alkaline earth metal and if appropriate reducing sugars. The nexus of the invention is the inclusion of a formate of an alkali metal or alkaline earth metal as part of the granule. Particularly preferred are calcium formate and sodium formate.

Water-insoluble fillers include cellulose, starch, cereal flour and the like (polysaccharides). However, as stated at column 2, lines 56 – 63, the enzyme granules usually comprise a mixture of cellulose and a laminar silicate or silicate mixture, if appropriate cereal flour and /or starch also being other constituents. Water-soluble filler mixtures include inorganic water-soluble salts. Binders, include polyethylene glycol and polyvinylpyrrolidone. The reference teaches “if” reducing sugars are to be used they include monosaccharides (glucose) disaccharides (lactose/maltose), and polysaccharides (dextrins). At column 3, lines 42 – 45, it is taught that the enzyme granule can comprise 0.5 to 15% by weight of a formate and if appropriate 0.5 to 20% by weight of reducing sugar. This is not Applicants’ enzyme granule. Additionally it is emphasized that the process of the reference for the preparation of the enzyme granule includes obtaining an extrudable composition obtained by mixing an enzyme concentrate with water, fillers, binders and if appropriate other constituents wherein the mixture is extruded to particles. Also at column 4, line 21 - 30 , it is taught that the enzyme concentrate may be added to a previously prepared dry pre-mix of the other constituents. Water is added and the composition is shaped and ready for extrusion.

Kiesser et al. does not teach or disclose a granule having a seed particle surrounded by a matrix including an enzyme in combination with a sugar or sugar alcohol and a polysaccharide structuring agent. For a reference to anticipate a claimed invention each and every element of the invention must be found in the prior art reference. Clearly the Kiesser et al. reference fails to teach not only Applicants’ claimed granules but also Applicants’ claimed method of producing said granules. Kiesser et al. is directed to an extrudable granule which includes an enzyme.

It is the Examiner’s position that all of the elements of Applicants’ invention with respect to the specified claims are instantly disclosed by the teachings of Scott (See page 4, pt 4 of the office action). Yet the Examiner also states that the Scott reference does not teach forming a granule over a seed particle and the presence of a coating layer over the granule. (see page 4, point 5 of the office action). However, it is the Examiner’s position if there are any differences between Applicants’ claimed methods and that of the prior art, the differences would appear to be minor in nature. The instant

claims are directed to a granule per se. As previously mentioned, restricted and non-elected claims reciting a method of preparing the claimed granules are presented in a separate divisional application. The instant granules comprise a) a seed particle and b) a protein matrix surrounding the seed particle; the matrix comprised of one or more proteins admixed with a combination of sugars or sugar alcohol and a polysaccharide structuring agent.

Applicants fail to understand how the cited reference anticipates the instant claims. The Scott reference does not teach or suggest an enzyme granule having a seed particle as a core surrounded by a protein matrix comprising an admixture of protein, sugar or sugar alcohol and a polysaccharide. Scott discloses specific particles which include an enzyme (glucose oxidase and optionally catalase), a sugar (glucose), a polysaccharide (cellulose), and optionally a synthetic polymer. As disclosed in the examples, the glucose and an aqueous solution of enzyme are combined to form an admixture, the moisture is then removed and the dried product is milled, pulverized or otherwise comminuted to reduce particle size. Additionally the surface of the particles may be coated with enzyme. For a reference to anticipate Applicants' claims there must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. Applicants submit the reference clearly does not anticipate an enzyme granule comprising a seed particle and a protein matrix surrounding the seed particle which comprises a protein admixed with a sugar or sugar alcohol and a polysaccharide.

Additionally, Applicants submit the reference does not make obvious the instantly claimed granule. There is no discussion in the Scott reference concerning a seed particle and a surrounding layer including a protein matrix. While the reference does disclose a free flowing particulate enzyme product, the particle product is (1) an enzyme (glucose oxidase) admixed with a sugar and optionally catalase or (2) an enzyme (glucose oxidase); a hydrolytic enzyme; and a low molecular weight polysaccharide (maltodextrin). The reference particles do not suggest either explicitly or implicitly the instantly claimed granules wherein an enzyme is admixed with a combination of a sugar or sugar alcohol and a polysaccharide structuring agent.

The Examiner rejected Applicants' claims as unpatentable over Markussen (EP 304332). This reference discloses a granule comprising a core surrounded by a coating comprising cellulose fibers or artificial fibers in an amount of 1.5 to 40% by weight, based on the dry weight of the granulate, except for the core. The core is disclosed as any coherent, non-crumbling material (inorganic or organic salts, starch, sugar or protein). In one preferred embodiment, the core and the coating contain enzymes which are different from each other. Additionally, the artificial fibers are made of polyethylene, polypropylene, polyesters, especially, Nylon, polyvinyl formal and poly(meth)acrylic compounds. Applicants' granule comprises a seed particle surrounded by a protein (enzyme) matrix including a protein (enzyme) admixture of one or more proteins, sugar or sugar alcohol, and a polysaccharide structuring agent. Markussen does not teach the combination of a sugar and a polysaccharide structuring agent in an admixture with one or more proteins.

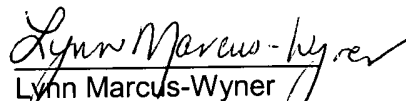
As stated at page 7, lines 11 – 20 of the disclosure, "it has not been possible previously to granulate enzymes in sugar or sugar alcohol since sugars and sugar alcohol exhibit "binder" characteristics, i.e. they are sticky and tend to plaster particles together (as happens intentionally in the case of granulation by agglomeration). ...Surprisingly, it has been found that by addition of a structuring agent to the sugar matrix formula, protein can be applied uniformly to individual seed particles at rapid rates without agglomeration or attrition."

There is no suggestion in the cited reference that an enzyme granule could include a surrounding layer around a seed particle or core which includes an admixture of protein, sugar or sugar alcohol and a polysaccharide structuring agent. The coating according to the cited reference may or may not include an enzyme in the coating and further includes 1.5 to 40% weight cellulose fibers or artificial fibers, 0 – 15% binders, a filler and one or more granulating agents. It is the inclusion of the polysaccharide structuring agent that helps with the stability of the granule. Further the sugar or sugar alcohol is critical in also providing stability of the granule.

Applicants contend instant claims 66 – 88 are patentable over the cited references, and allowance of said claims is kindly solicited. If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 846-7620.

Respectfully submitted,

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